REMARKS

I. Introduction

The Applicants would like to acknowledge with thanks the telephonic interview of August 12, 2003, during which the instant claim amendments were discussed. Claims 1-5, 7-9, 11-37, and 40 are pending in the instant application. New claim 41 is presented.

II. The rejection of claims 1-5, 7-9, 11-37 and 40 under the judicially created doctrine of obvious-type double patenting should be withdrawn.

The Examiner rejected claims 1-5, 7-9, 11-37 and 40 under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over claims 8-13 of U.S. Patent No. 6,361,946 (hereinafter "the '946 patent").

Solely to expedite allowance, Applicants file herewith a Terminal Disclaimer. Accordingly, the rejection of claims 1-5, 7-9, 11-37 and 40 should be withdrawn. The Applicants reserve the right to demonstrate patentable distinctness between the claims sets.

III. The rejection of claims 5, 7-9, and 11-18 under 35 U.S.C. 112, first paragraph, should be withdrawn.

The Examiner rejected claims 5, 7-9, and 11-18 under 35 U.S.C. 112, first paragraph, alleging that the specification fails to provide enablement for a method of treatment of a patient in need of modulation of Flt4 activity. The Examiner recommended that the Applicants cancel the phrase "identification of patients" to overcome the rejection.

Because the suggestion expedites allowance and does not narrow the claims, the Applicants have amended claim 5 as suggested by the Examiner. Specifically, claim 5 has been amended to delete the phrase "comprising the steps of: identifying a patient in need of modulation of Flt4 activity; and." Dependent claims 7-9 were correspondingly amended to reflect the amendment to claim 5. The assertion by the Examiner that "...there are no limitations which patients are included

and which are excluded and no guidance provided to predictably determine which patients may benefit and which may not" does not apply to amended claim 8 which recites the limitation of patients suffering from a disorder of the lymphatic system. Thus, a specific patient population is identified in amended claim 8.

The specification as filed teaches that Flt4 is expressed on (and becomes largely restricted to) lymphatic vessels (see p. 4, line 21, to p. 5, line 2), and that the patients in need of modulation of their lymphatics are candidates to receive the Flt4 ligand taught in the application:

> The biological effects of VEGF-C on lymphatic endothelia indicate *in vivo* uses for polypeptides of the invention for stimulating lymphangiogenesis (e.g., to promote re-growth or permeability of lymphatic vessels in, for example, organ transplant patients; to mitigate the loss of axillary lymphatic vessels following surgical interventions in the treatment of cancer (e.g., breast cancer); to treat aplasia of the lymphatic vessels or lymphatic obstructions) and for inhibiting it (e.g., to treat lymphangiomas). Additional *in vivo* uses for polypeptides of the invention include the treatment or prevention of inflammation, edema, elephantiasis, and Milroy's disease.
>
> (Page 21, lines 3-10. See also Example 29 on page 82, lines 14-19)

Example 29 of the specification shows that VEGF-C promotes lymphatic vessel growth. Thus, the specification as filed identifies a variety of patients that will benefit from Flt4 modulation in contexts related to the lymphatics.

Similarly, newly added claim 41 recites identifying a patient in need of modulation of myelopoiesis. As discussed above with respect to the amendment to claim 8, the basis of the Examiner's rejection for failure to provide enablement for a method of treatment of a patient in need of modulation of Flt4 activity does not apply since new claim 41 is limited to a defined patient population. As pointed out to the Examiner in the Applicant's last response, the application teaches use of the Flt4 ligand VEGF-C to stimulate myelopoiesis in a mammalian subject in need of modulation of myelopoiesis. For example, the specification as filed teaches the use of the Flt4 ligand VEGF-C to stimulate myelopoiesis in a mammalian subject suffering from granulocytopenia. (Page 22, last paragraph.) These teachings are supported in

part by the teachings in Example 36 that a population of CD34+ progenitor cells express Flt4 (VEGFR-3). (See, e.g., p. 102, lines 14-21)

The foregoing amendments raise no new issues since the subject matter of claims 8 and 41 have previously been argued in the prior response (See, e.g., Paper No. 14, dated February 28, 2003, page 4) and were not disputed by the Examiner in the final Office Action. Accordingly, the rejection of claims 5, 7-9, and 11-18 under 35 U.S.C. 112, first paragraph, should be withdrawn.

IV. The rejection of claim 22 under 35 U.S.C. 112, first paragraph, should be withdrawn.

Claim 22 was rejected under 35 U.S.C. 112, first paragraph, for allegedly containing subject matter that was not adequately described in the specification to enable one skilled in the art to make and/or use the invention.

In response, the Applicants have filed a Budapest Treaty Declaration, attached as Appendix A hereto. This declaration was previously filed in related U.S. Patent Application Serial No. 08/585,895, now U.S. Patent No. 6,245,530. This declaration, which pertains to identical deposited material as in the instant application, satisfies the requirements of 37 CFR 1.801 through 1.809. Accordingly, the Applicants respectfully request that the rejection of claim 22 under 35 U.S.C. 112, first paragraph, be withdrawn.

V. The rejection of claims 19-27 under 35 U.S.C. 112, first paragraph, should be withdrawn.

The Examiner rejected claims 19-27 under 35 U.S.C. 112, first paragraph, alleging that the claims encompass gene therapy, yet the specification, while being enabling for a method of stimulating endothelial cell growth comprising administering a polypeptide comprising the amino acid sequence of SEQ ID NO: 8 and variants thereof, does not reasonably provide enablement for gene therapy using nucleic acids encoding these polypeptide fragments.

In response, the Applicants have canceled claims 19-27 with the intention of pursuing the subject matter therein in a divisional application. Accordingly, the rejection under Section 112 should be withdrawn.

CONCLUSION

For the foregoing reasons, reconsideration and withdrawal of all rejections and objections is requested. However, if the Examiner has questions, or identifies any remaining issues preventing allowance that might be resolved by a telephonic interview or examiner's amendment, the Applicants request and invite the examiner to telephone the undersigned attorney to resolve such questions or issues.

Respectfully submitted,

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Dated: August 20, 2003

By: 

David A. Gass
Registration No. 38,153

OFFICIAL

APPENDIX A

BUDAPEST TREATY DECLARATION

PATENT
28967/33072

IN THE UNITED STATES
PATENT AND TRADEMARK OFFICE

In re Application of:

Alitalo et al.

Serial No.: 08/585,895

Filed: January 12, 1996

Title: RECEPTOR LIGAND

Art Unit: 1801

Examiner: Lathrop, B.

I hereby certify that this paper is being deposited with the United States Postal Service as first class mail, postage prepaid, in an envelope addressed to: Assistant Commissioner for Patents Washington, D.C. 20231, on this date:

Dated: Nov. 26, 1997

David A. Gass
Registration No. 38,153

DECLARATION OF BIOLOGICAL CULTURE DEPOSIT IN COMPLIANCE WITH BUDAPEST TREATY REQUIREMENTS

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

I, the undersigned, declare that:

1. I am an inventor of the subject matter of the above-identified patent application.

2. The plasmid designated FLT4-L, described in the specification of the above-identified application at pages 28-29 (and elsewhere), was deposited on 24 July 1995 with the American Type Culture Collection (ATCC), 12301 Parklawn Drive, Rockville, Maryland 20852, under the terms of the Budapest Treaty. This plasmid was assigned ATCC accession number 97231. A copy of the ATCC deposit receipt, confirming viability of the deposit, is attached hereto.

3. With respect to the permanence of the deposit, the ATCC is an official depository in accordance with the Budapest Treaty for the above-deposited material, and I affirm that, should the plasmid identified in paragraph 2 mutate, become non-viable, or be inadvertently destroyed, I will replace it for at least thirty (30) years from the date of the original deposit, or for at least five (5) years from the date of the most recent request for release of a sample, or for the enforceable life of any patent issued on the above-mentioned application, whichever period is longest.

4. With respect to availability of the plasmid identified in paragraph 2, I affirm that the deposit has been made under conditions of assurance of (a) ready accessibility thereto by the public if an enforceable patent is granted whereby all restrictions to the availability to the public of the culture so deposited will be irrevocably removed upon the granting of the patent [MPEP §608.01 (p)], and (b) access to the deposit will be available during pendency of the patent application to one determined by the Commissioner to be entitled thereto under 37 C.F.R. §1.14 and 35 U.S.C. §122.

5. I hereby further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code, and that such willful, false statements may jeopardize the validity of the application or any patent issued thereon.

November 20, 1997
Date

Kari Alitalo

American Type Culture Collection

12301 Parklawn Drive • Rockville, MD 20852 USA • Telephone: (301)231-5520 Telex: 898-055 ATCCNORTH • FAX: 301-770-2587

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3 AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

University of Helsinki
Attention: Kari Alitalo
Molecular/Cancer Biology Laboratory
P.O. Box 21 (Haartmaninkatu 3)
SF-00014, HELSINKI, FINLAND

Deposited on Behalf of: Kari Alitalo and Vladimir Joukov

Identification Reference by Depositor:	ATCC Designation
Plasmid, FLT4-L	97231

The deposit was accompanied by: __ a scientific description __ a proposed taxonomic description indicated above.

The deposit was received July 24, 1995 by this International Depository Authority and has been accepted.

AT YOUR REQUEST:

X We will not inform you of requests for the strain.

The strain will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strain and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strain.

If the culture should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace it with living culture of the same.

The strain will be maintained for a period of at least 30 years after the date of deposit, and for a period of at least five years after the most recent request for a sample. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the culture cited above was tested August 1, 1995. On that date, the culture was viable.

International Depository Authority: American Type Culture Collection, Rockville, Md. 20852 USA

Signature of person having authority to represent ATCC:

Annette L. Bade, Director, Patent Depository

Date: August 9, 1995

cc: Thomas C. Meyers